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COMMENTARY

Fostering responsible research practices is a shared responsibility of multiple stakeholders

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1. Introduction

In their recent commentary, Wallach et al. explain that breaches of research integrity will typically do damage to the reliability and validity of biomedical research [1]. This may harm regulatory and clinical decision-making. Consequently health care and public health may suffer. They point out that prevalent questionable research practices like poor study design, low power and selective reporting probably do substantially more damage than the rare occurrence of the classical ''deadly sins'' of fabrication, falsification, and plagiarism. Wallach et al. do not dwell much on the causes of the shortcomings listed in their table 1 and take the view that the remedy should come from better guidelines, more transparency, and mandatory training [1].

While I agree with all this, I would like to strengthen the argumentation by first analyzing the replicability crisis and the need for more transparency a bit further. Second, I shall explore what biomedical research can learn about fostering responsible research practices from other disciplines, social sciences first and foremost. Finally, the putative determinants of research misconduct and questionable research practices will be discussed, and the actions different stakeholders can take shall be explored.

2. Replicability crisis

A 2012 Nature publication showed the reproducibility of oncological animal studies to be embarrassingly low [2]. Also for other types of research, reproducibility rates between 10% and 40% are reported [3]. This is no surprise for methodologists, as some of the background was already pointed out in the classical article ''Why most research findings are false'' [4]. Next to low power and flawed study design, especially, selective reporting of positive results may be the most important driver of the replicability crisis.

We do not yet have a clear view on what we exactly mean when we say that a study is replicated [5]. We also do not know how common the problem is and what would be the most effective ways to deal with it. A common prejudice seems to be that replication is a second rate activity for investigators not bright enough to do innovative work. But that might not be true given the abundance of good quality applications for the research program on replication studies of the Netherlands Organisation for Scientific Research [6]. Interestingly, the field of clinical trials may be an exception in the sense that large prospectively registered well-designed multicentre trials may be quite reproducible. In this arena, even redundant replication may be an issue as can be illustrated in cumulative meta-analyses [7].

Wallach et al. point correctly out that there is still substantial room for improving the reliability and validity of clinical trials as the fundament of regulatory and clinical decision-making [1]. My point is that the situation is probably much worse in observational etiologic, diagnostic, and prognostic research. And also that these fields can learn a lot from the decades of experience in making randomized clinical trials more reliable and more valid.

3. Need for more transparency

Although the compliance should be improved further, prospective trial registration is the example that can most likely help other fields to fight selective reporting and to improve replicability. In its full version, the idea is that complete study protocols need to be deposited before the start of data collection [8,9]. Later changes are possible, but will leave traces and might be considered data-driven.

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Also, the data analysis plan must be uploaded before the statistical analyses start. And after the study, the archive needs to be completed by adding the log of data collection, the syntaxes of the analyses, the full data set and its code book, and all results. It is debatable if and when the elements of this archive must be publicly accessible. And if not under which conditions and to whom access will be granted. To be able to practice transparency, a number of conditions have to be met, such as having the essential skills and facilities, and the means to adequately protect the identity of study participants. And there may be negative side effects of making data public, like *mala fide* misuse of data sets. For a fuller discussion, I refer to the ten commentaries on transparency that appeared in the February 2016 issue of this journal [10].

We should realize that the practice of transparency in the sense outlined previously concerns the tradition of hypothesis testing research. The essence of exploratory research is that the next steps in the project are data-driven; therefore, having a fixed study protocol is not useful. In exploratory research ''anything goes'', as long as it is clearly reported what has been done, and no conclusions are drawn on the emerging (*post hoc*) hypotheses.

Please note that the need to be transparent and to fight the lack of replicability and selective reporting are also the core elements in the Lancet REWARD Campaign that has many university medical centers and biomedical funding agencies as signatories [11]. The core idea is simple and started by an analysis that argued that 85% of clinical research may be wasted [12]. The reasons for that being avoidable were because the studies at issue have (1) irrelevant research questions, (2) poor research methods, (3) selective reporting, or (4) poor reporting quality. The last point links to the many ($N = 376$) useful reporting guidelines that are currently available for biomedical research and conveniently made accessible by the Enhancing the QUAlity and Transparency Of health Research (Equator) Network [13].

4. What can be learned from the neighbors?

Although biomedical research is important and may concern about half of the research volume worldwide, there exist other academic disciplines and their experiences with research misconduct, questionable research practices, and replication problems might be different. Biomedical research can learn from that and might consider adoption of effective solutions developed by its disciplinary neighbors. Although the evidence is thin, it seems that qualitative empirical research and hermeneutic and reflective approaches that are prevalent in the Humanities and in Law schools suffer from partly other threats to reliability and validity. Plagiarism, selective use of sources, and lack of transparency in the various steps of the argumentation seems to be relatively important in these domains. And in the natural sciences, replicability may be less a problem than elsewhere due to its tradition of internal replication, intense international collaboration, publishing preprints, and making available data sets to interested colleagues. For a comprehensive orientation, I recommend the recent report on *Fostering Integrity of Research* by the US National Academies of Science [14] and the European Commission briefing article on *Research Integrity: What it Means, Why it Is Important, and How we Might Protect it* [15].

A lot of inspiring work has been done in the Social Sciences. In a way it started with the case of data fabrication by Diederik Stapel that deeply shocked both the general public and scientists. An excellent investigation report appeared [16], and Tilburg University and the social sciences at large responded with important improvements and preventive measures. Recently, Klaas Sijtsma, who succeeded Stapel as dean of the School of Social and Behavioral Sciences at Tilburg University, presented a keynote lecture on the 5th World Conference on Research Integrity (WCRI) with the telling title ''Never waste a good crisis'' [17].

Another game changer in social science was the 2015 Science publication on ''Estimating the reproducibility of psychological science'' [18]. That made clear that on replication, the effect size of 100 ''cornerstone publications'' were only half of the initial magnitude, and the proportion of significant studies deceased from 97% to 36%. This lead to intensive soul searching and gave substantial momentum to the Center of Open Science [19] that introduced a number of highly relevant improvements like the Open Science Framework [20], the Transparency and Openness Promotion guidelines [21,22], and Registered Reports [23,24]. Recently, the ''Manifesto for Reproducible Science'' was published, highlighting the practical measures that most likely would help in solving the issues [25]. These developments could inspire further improvements in biomedical research. Also, the concept of ''researcher degrees of freedom'' and the need to restrict these as much as possible seems very relevant for biomedical research [26].

5. Determinants of research misbehavior

Ideally, interventions to prevent, diagnose, or treat the various forms of research misbehavior should be based on evidence on its most important determinants. Unfortunately, so far the evidence is scarce, and the field of ''meta-research'' is still in its infancy. The good news is that this seems to change fast, with increasing funds for research (e.g., in the European Union Horizon 2020 program [27] and programs on Fostering Responsible Research Practices [28] and Replication Studies [6] in the Netherlands). Also, research institutes are emerging, similar to the Collaboration for Research Integrity and Transparency [29], were Wallach et al. are based, the

Meta-Research Innovation Center at Stanford [30], and the Meta-Research Center at Tilburg University [31].

Having said that, we do have some insights in what the most likely root causes of the various research misbehaviors actually are [14,15]. The big picture seems to be that scientists experience dilemmas and conflicts of interest in daily practice that arise from the fact that what is good for the validity and reliability of science is not always good for their personal career. Many rewards are linked to having positive and spectacular results as these are published more easily in high impact journals and will be cited more often. The various forms of research misbehavior have in common that they can help to get positive and spectacular results. Thus, the current reward criteria in science act partly as perverse incentive. It also seems likely that determinants of research misbehavior are manifold and can concern the individual researcher, the research climate in with he or she works, and the system of science at large.

At the level of the science system, perceived organizational injustice due to almost exclusively rewarding positive and spectacular results seems to play an important role, as is the perceived (low) likelihood of being caught by reviewers or colleagues. Important determinants connected to the research climate may be perceived norm adherence, level of competition and level of social support in the group, and the quality and intensity of mentoring and supervision. At the level of the individual scientist, important determinants of research misbehavior may be the dependency on external funding, perceived work pressure, and personal norm subscription. Unfortunately, the evidence on most of these determinants is weak, and they have never been studied simultaneously.

6. There is no magic bullet

Taking all this together, it seems reasonable to conclude that (1) there are serious problems we need to fix in science, (2) multiple stakeholders have a role to play, (3) the evidence-base for this needs further strengthening, and (4) we should exchange experiences and learn from each other [32,33]. Although individual scientists are responsible for their own behavior and any minor or major breaches of research integrity they commit, we need to recognize that research institutions, funding agencies, and scientific journals can and should take measures to foster responsible research practices and to detect and handle instances of major or minor research misbehaviors.

Research institutions have the duty to have clear codes and procedures regarding research integrity, and to ensure good facilities, adequate mentoring, and training in responsible conduct of research at all levels [34]. Specific arrangements must be made to enable transparency and to monitor research quality, such as good data management and storage facilities, adequate methodological and statistical support, and a system of internal audits. Institutions should tackle the perverse incentives in their reward systems and promote a research climate in which dilemmas can be openly discussed, and learning from mistakes is encouraged. Institutions may decide to explore the salient aspects of their research climate and identify promising ways to promote responsible conduct of research by consulting their community of researchers. An example is the ongoing project Academic Research Climate in Amsterdam that involves two universities and two university medical centers [35].

Funding agencies should demand that research institutions fulfill their duties of care in the sense outlined previously. They should also make transparency ‘‘from protocol to publication’’ obligatory and be clear about the required level of open access and open data. All research proposals should convincingly argue that the research question is relevant and not yet sufficiently studied. Funding agencies need to strike an adequate balance between innovation and replication in their portfolio and also offer grants for meta-research. With a clever mix of ‘‘sticks and carrots’’ funding agencies can have a profound impact on the behavior of researchers and their institutions [36].

Scientific journals have a key role in preventing selective publication and in promoting reporting quality. They should consider adoption of Registered Reports as this is an effective way to focus solely on the relevance of the research question and the soundness of the methods, and to avoid being distracted by the results of the study [23,24]. This is done by first submitting the introduction and methods sections and starting data collection only when the article is accepted for publication on the condition that the study is performed as planned and adequately reported. Scientific journals should adopt as much as possible the Transparency and Openness Promotion guidelines [21,22] and enable and encourage postpublication peer review.

Research integrity is an important issue for all disciplinary domains, for all regions and countries in the world, and for multiple stakeholders. The scarcity of good quality evidence and the rapid rate at which the field is evolving make it necessary to exchange experiences, to identify best practices, to collaborate, and to align interventions. For this, both national and international platforms are emerging. An example of a national platform is the Netherlands Research Integrity Network [37]. Netherlands Research Integrity Network organizes symposia on responsible conduct of research education and on meta-research, convenes closed meetings for confidential counselors and committee members involved in handling allegations of breaches of research integrity, and maintains a website that offers a wealth of information on these topics.

An example of an international platform is the series of World Conferences of Research Integrity the fifth of which was held in Amsterdam in 2017 [38]. After the event, the conference website was enriched with PDFs of almost all presentations and videos of the keynote lectures. The 2nd WCRI yielded the Singapore Statement that is taken as anchor by many national and international codes of conduct [39]. The

5th WCRI adopted the Amsterdam Agenda that specifies the need to register meta-research and to evaluate the efficacy of all measures and interventions aimed at fostering research integrity [40]. The idea is that the research integrity community should practice what it preaches and make a strong plea for evidence-based policies.

To return to the jargon of clinical research, there is no magic bullet. We need a mix of different interventions to prevent breaches of research integrity, detect and handle cases of misbehavior, and to foster responsible research practices. Interdisciplinary and international collaboration and exchange of best practices, that includes all relevant stakeholders, should form the basis of rapid progress.

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